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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/493,484	01/28/2000	Adriaan Anthonius Wilhelmus Marie Van Loon	1999.454 US	2307

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EXAMINER	
PARKIN, JEFFREY S	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/493,484	VAN LOON, ADRIAAN ANTHONIUS WILHELMUS M	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 03 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 07 November, 2003

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 5-9, 14, 16, 17, 24, + 25 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) 14 is/are allowed.

6)☒ Claim(s) 5-9, 16, 17, 24, +25 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Office Action

37 C.F.R. § 1.114

A request for continued examination under 37 C.F.R. § 1.114, including the fee set forth in 37 C.F.R. § 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. § 1.114, and the fee set forth in 37 C.F.R. § 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R. § 1.114. Applicant's submission filed on 07 November, 2003, has been entered. Claims 5-9, 14, 16, 17, 24, and 25 are currently under examination.

35 U.S.C. § 112, Second Paragraph

Claims 5-9, 16, 17, 24, and 25 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant. The claims are confusing since it is not readily manifest if the Mab accession nos. actually refer to purified antibodies, deposited hybridoma cell lines, bacterial cultures (i.e., producing recombinant Abs), or eukaryotic cell lines encoding expression vectors producing the Abs of interest. Perusal of the disclosure appears to suggest that said accession nos. reference hybridoma cell lines that produce the Mabs of interest. Appropriate correction is required (i.e., ... wherein antigens from said ERS isolate are not recognized by the Mabs INT 13-06, INT 14-11, and 15-01 INT ...).

35 U.S.C. § 112, First Paragraph

1. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 5-9, 16, 17, 24, and 25 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). The claims have been amended and are now directed toward a vaccine comprising avian reovirus ERS isolates. These isolates induce polyclonal antiserum in a host and said antiserum is capable of inhibiting plaque formation by the wildtype ERS isolates (ECACC No. 99011475) by at least 75%. The viruses employed in the vaccine composition also react positively with polyclonal antisera but not with three designated monoclonal antibodies (Mabs '472, '473, '474).

As previously set forth, in order to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Vas-Cath, Inc., v. Mahurkar*, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116. The issue raised in this application is whether the original application provides adequate support for the broadly claimed genus of avian reovirus ERS isolates that are present in the vaccine composition. An applicant

shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the biomolecule of interest. *In re Bell*, 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993). *In re Deuel*, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995). A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 U.S.P.Q.2d 1895, 1905 (Fed. Cir. 1995). The court noted in this decision that a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not reasonably lead those skilled in the art to any particular species.

An applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant

was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. For some biomolecules, examples of identifying characteristics include a nucleotide or amino acid sequence, chemical structure, binding affinity, binding specificity, and molecular weight. The written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. Without such a correlation, the capability to recognize or understand the structure form the mere recitation of function and minimal structure is highly unlikely. In the latter case, disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement. *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404, 1406 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998). *In re Wilder*, 736 F.2d 1516, 1521, 222 U.S.P.Q. 369, 372-3 (Fed. Cir. 1984). Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

The disclosure fails to provide adequate guidance pertaining to a number of these factors as follows:

1) The disclosure fails to provide the complete nucleotide or amino acid sequence of any given avian reovirus ERS isolate. While it is noted that the disclosure describes the isolation and preliminary characterization of a single avian reovirus (designated ERS) bearing the E.C.A.C.C. accession no. 9901475, this is the only

virus that was isolated in the specification. **Nucleotide and amino acid sequence data was not provided for this isolate or any other isolate.** Thus, the disclosure clearly fails to provide the structure, or any critical molecular determinants, that modulate the phenotypic properties of any given ERS isolate.

2) The phenotypic properties used to describe the claimed invention fail to provide any further illumination pertaining to the genotypic properties of any given isolate. Limitations are directed toward the ability of any given virus to induce antiserum in an animal that produces a certain degree of plaque reduction when measured in an art-recognized plaque reduction assay. Another defining property is directed toward a negative limitation that simply specifies that the avian reovirus of interest does not react with a small group of monoclonal antibodies of undefined specificity. However, these simple defining criteria fail to provide any guidance pertaining to the genotype of any given isolate. Thus, the skilled artisan has been asked to guess as to which isolate might meet the claimed limitations.

3) The disclosure fails to provide any clear correlation between the genotype and phenotype of any given reovirus. For instance, the claimed genus of ERS isolates is being defined by their ability to induce antisera with a certain neutralizing activity. However, the disclosure fails to provide any correlation between the induction of said antisera and corresponding genotypic/phenotypic changes in the reoviral genome. The disclosure fails to identify any critical antigenic or immunogenic determinants. Nothing in the disclosure would lead the skilled artisan to any particular isolate other than the one bearing the ECACC designation 9901475. Thus, the skilled artisan cannot readily ascertain if they are in possession of the claimed invention.

4) The disclosure fails to provide a reproducible method for making a homogenous population of avian reoviruses with similar structures

and functions. The avian reovirus of interest was isolated from chickens having digestive problems and passaged on a suitable cell line. The ability of this virus to induce neutralizing antisera was assessed using a plaque reduction assay. However, this assay fails to provide any guidance pertaining to the molecular determinants that modulate the desired phenotype of the virus. It has been well-documented that **the avian reoviruses display considerable genotypic/phenotypic heterogeneity (Nersessian *et al.*, 1989; Rosenberger *et al.*, 1989; Patrick *et al.*, 2001; Jones, 2002; Kapczynski *et al.*, 2002).** Thus, using the described methodology, the skilled artisan can only guess as to what the final product will be.

When all the aforementioned factors are considered *in toto*, the skilled artisan would reasonably conclude that applicants were not in possession of the claimed invention. The skilled artisan would conclude that applicants were in possession of a single avian reovirus ERS isolate having the E.C.A.C.C. accession no. 9901475. It is also noted that reference is made to ERS isolates 2 and 3. However, it is not clear if these isolates were deposited and detailed phenotypic characterizations performed.

Response to Arguments

3. Applicant provides a number of arguments, many of which were previously set forth, as follows: 1) The art recognizes the characterization of viruses by their antigenicity. 2) The disclosure provides numerous examples of isolated avian reoviruses with the defined characteristics. 3) Applicant contends that the case law relied upon fails to support a *prima facie* case for lack of written description.

Concerning the first point, the Examiner does not dispute the finding that serological properties of are often used in the classification of viruses. However, merely citing a particular

immunological property without a further understanding of the molecular determinants modulating that activity fails to provide any further illumination pertaining to the genotype of any given isolate. Applicants are attempting to define a large genus of genotypically/phenotypically independent and distinct viruses based upon a rather generic assay. The assay relied upon fails to provide the skilled artisan with any guidance pertaining to the genotypic modifications that impart those properties to any given isolate. This is why those skilled in the art rely upon several properties, in addition to serology, to identify and classify any given virus or isolate. Additional properties routinely employed include virion morphology (e.g., virion size, virion shape, presence of absence of an envelope, capsid symmetry and structure), physicochemical properties (e.g., virion molecular mass, virion buoyant density, pH stability, cation stability, solvent stability, detergent stability), genomic characteristics (e.g., type of nucleic acid, genome size, strandedness, linearity, segmentation, nucleotide sequence, G/C content, presence of 5' terminal cap, presence of 5' terminal covalently linked protein), proteins (e.g., number, size, structural functions, nonstructural functions, amino acid sequence, posttranslational modifications), lipid content, carbohydrate content, genome organization and replication strategies, antigenic properties, and biologic properties (e.g., host range, mode of transmission, vector relationships, tissue tropism). The claim language fails to incorporate any meaningful structural or functional limitations that would readily allow the skilled artisan to identify whether or not they were in possession of the claimed subject matter.

Concerning the second point, while it appears that more than one ERS isolate was identified (e.g., see Table 3, p. 19), nevertheless, only one specific isolate was deposited (ECACC No. 99011475). The disclosure fails to provide any detailed structural

or functional characterizations of these other isolates. The disclosure fails to provide a single replication-competent molecular clone. The disclosure fails to provide detailed nucleotide sequence analyses from any of the isolates, including the deposited isolate. Thus, the skilled artisan cannot even begin to ascertain the coding potential of any given isolate. The skilled artisan cannot even begin to ascertain which genomic segments, and the modifications contained therein, that are responsible for the desired phenotype of the virus. Thus, the skilled artisan would reasonably conclude that applicants were in possession of a single avian reovirus, which has the ECACC designation no. 99011475. If additional ERS isolates have been deposited with an appropriate agency, the Examiner would consider appropriate drafted claim language directed toward these embodiments (i.e., A vaccine comprising an avian reovirus ... which is deposited at the ECACC under accession no. XXXXXXXX).

Concerning the third point, the case law relied upon in the rejection is directly relevant. As previously set forth, an applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. For some biomolecules, examples of identifying characteristics include a nucleotide or amino acid sequence, chemical structure, binding affinity, binding specificity, and molecular weight. The written description

requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. Without such a correlation, the capability to recognize or understand the structure form the mere recitation of function and minimal structure is highly unlikely. In the latter case, disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement. *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404, 1406 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998). *In re Wilder*, 736 F.2d 1516, 1521, 222 U.S.P.Q. 369, 372-3 (Fed. Cir. 1984). Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. The aforementioned citations are not strictly limited to nucleic acids, but provide generally applicable principles to be used in assessing whether any given inventions meets the legal criteria set forth under this statute. The claimed invention is directed toward a large genus of poorly defined avian reoviruses. Contrary to applicant's assertion, the claims are not directed toward a "living" organism but are directed to a virus. Viruses are not capable of replication in the absence of a host. However, the *sine qua non* of any given virus is its genome and the proteins encoded thereby. So in essence, the claims are really directed toward an aggregation of "biomolecules" whose various properties contribute to the final phenotype. The phenotypic properties of any given virus are influenced by these various proteins. The reoviruses contain 10 dsRNA genome segments within a non-enveloped, icosahedral double capsid. These segments can be further divided into large (L1, 2, 3), medium (M1, 2, 3),

and small (S1, 2, 3, 4). The disclosure fails to provide any guidance pertaining to changes within any of these segments that correlate with the claimed phenotypic properties of the generic class of avian reoviruses. Applicant has no knowledge or understanding of which segments are critical for the desired phenotype. Thus, the applicant has clearly failed to meet the burden required under this statute. The law requires the invention to be clearly defined. Applicant has failed to provide sufficient defining criteria.

Applicants also proffered three references in support of their arguments (Estes *et al.*, 1980; Green *et al.*, 1988; Kang *et al.*, 1993). The Estes publication used a plaque-reduction assay to distinguish between simian, bovine, and porcine rotavirus isolates. All of these isolates are infect different mammalian species and would be expected to display considerable genotypic and phenotypic heterogeneity. However, this reference does not describe the usefulness of plaque reduction assays in characterizing closely related rotavirus isolates. Moreover, the authors also note that it is critical to employ a well-characterized, high-titer, high-quality antisera. The claimed invention does not set forth any such stipulations. In fact, the specification clearly illustrates the difficulties associated with using plaque reduction assays to characterize different viruses. The claims require a 75% reduction in plaque formation. Interestingly, all of the reovirus isolates (ERS and non-ERS) described in the specification met this limitation (see p. 17, Table 2A). Green and colleagues characterized human rotavirus field isolates by direct sequence analysis of the VP7 gene. These results were correlated to one of four known serotypes. The Examiner does not dispute the notion that a panel of well-characterized monoclonal antibodies can be utilized to ascertain the serotype of particular reovirus isolates. However, the key to effective serotyping is to have a panel of

well-characterized monoclonal antibodies of defined specificity. The instant application fails to describe such a panel. Kang and associates also performed serotyping studies involving human and porcine rotaviruses. Once again, most of the Mabs employed were useful in distinguishing between reoviruses of different animal origins, but were less discrimination between viruses of the same origin. For instance, Kang and colleages clearly state that Mab RG36H9 failed to distinguish between porcine serotypes G3 and G4. Thus, it is imperative to employ a panel of well-characterized Mabs in attempting to serotype any given virus strain. However, the disclosure fails to provide such a panel.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 9:30 AM to 7:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, Laurie Scheiner or James Housel, can be reached at (571) 272-0910 or (571) 272-0902, respectively. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

21 February, 2004